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| APPLICATION NO. | FILING DATE | FIRST-NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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EXAMINER

LI, RUIXIANG

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 08/11/2003

[Handwritten signature]

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/944,884

Applicant(s)

BAKER ET AL.

Examiner

Ruixiang Li

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-41 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 22-27,30,31 and 35-41 is/are rejected.
- 7) ☒ Claim(s) 28,29 and 32-34 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Claims and Status of the Application

1. Applicants' amendment in Paper No. 3, 4, and 7 has been entered in full. Claims 1-21 have been canceled. Claims 22-41 have been added. Claims 22-41 are pending and under consideration.

Priority

2. Based on applicants' priority statement in Paper No. 7, filed on September 3, 2003 and an inspection of the parent applications, the Examiner has concluded that the subject matter defined in this application is supported by the disclosure in U. S. Application Serial No. 09/254,311, filed on March 3, 1999, which is a 371 of PCT/US98/25108, filed on 12/01/1998, but is not supported by a U. S. Provisional application 60/069,334, filed on 12/11/1997. This is because Application No. 60/069,334 fails to provide a patentable utility for the instantly claimed invention and thus it does not enable one skilled in the art to use the claimed invention. Accordingly, the subject matter defined in claims 22-41 has an effective filing date of 12/01/1998.

Should applicants disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent applications filed prior to 12/01/1998, which specifically

support the claimed subject matter defined in the instant application for each pending claim.

Drawings

3. The drawings filed on August 31, 2001 are accepted by the Examiner.

Information Disclosure Statement

4. The information disclosure statement filed on April 29, 2002 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. The information on the references listed in PTO-1449 form is incomplete. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that *a new PTO-1449 form be submitted for the application* and that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Claim Rejections—35 USC § 112, 1st paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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6. Claims 22-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a polypeptide of SEQ ID NO:2 (referred to as PRO241), does not reasonably provide enablement for an isolated nucleic acid having at least 80%-99% amino acid sequence identity or hybridizing to the nucleic acid encoding the polypeptide of SEQ ID NO:2 or to the nucleic acid sequence of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The claims are drawn to an isolated nucleic acid having at least 80%, 85%, 90%, 95% or 99% sequence identity or hybridizing to a nucleic acid sequence encoding the polypeptide set forth in SEQ ID NO:2 or its fragments, to the nucleic acid sequence of SEQ ID NO: 1, or to the full-length coding sequence of the cDNA deposited under ATCC Accession No. 209526. Thus, the claims encompass a huge number of nucleic acids that vary substantially both in length and in nucleotide composition. In particular, claims 35-37 encompass virtually any random nucleic acid sequence of any length because the claims have no recitation of specific

hybridization conditions and any nucleic acids could hybridize to the recited nucleic acids.

Since there is no functional limitation in the claims, the claims encompass an unreasonable number of inoperative nucleic acids, which an artisan would not know how to use. The specification discloses that the polypeptide of SEQ ID NO:2 encoded by the nucleic acid of SEQ ID NO: 1 is a secreted protein and has homology to the biglycan protein (page 2) and Applicants have taught the polypeptide consisting of the mature form of SEQ ID NO:2, as well as the putative signal sequence (amino acid residues 1-15 of SEQ ID NO:2; Figure 2). PRO241 polypeptide was shown to stimulate the release of proteoglycans from cartilage (page 137, Example 29). However, why the polypeptide stimulates the release of proteoglycans from cartilage is not disclosed. Since PRO241 is a secreted protein, it would be expected that the mature form would be sufficient for function in the absence of the secretory signal. As opposed to the claims, what is disclosed about PRO241 is narrow: a single nucleic acid of SEQ ID NO: 1 and a single polypeptide of SEQ ID NO: 2 with one disclosed function and no other obvious specific functions. The skill in this area of work is not high because no art teaches the instantly claimed nucleic acids or analogues. It is noted that an art, after the effective filing date teaches an nucleic acid encoding an amino acid sequence which is 100% identical to SEQ ID NO:2 (Lorenzo et al, Identification and characterization of asporin. A novel member of the leucine-rich repeat protein family closely related to decorin and biglycan. *J. Biol. Chem.* 276:12201-12211, 2001). However, even this art does not provide any information how to make and use the claimed broad genus of nucleic acids.

There are no working examples of using nucleic acids that encode polypeptides that are less than 100% identical to the polypeptide SEQ ID NO:2 or the mature form thereof. There is only function attributed to PRO241: stimulation of the release of proteoglycans from cartilage (page 137, Example 29). An artisan would not know how to use non-identical nucleic acids on the basis of teachings in the prior art or specification unless they possessed the activity disclosed in the instant specification. While the specification generally describes properties of secreted proteins, it is acknowledged that such secreted proteins are diverse in function and structure (See, e.g., page 1 of the instant disclosure). The specification does not provide guidance for using polypeptides encoded by the claimed nucleic acids, which do not have the single specific disclosed activity disclosed for PRO241. The claims are broad because they do not require the claimed nucleic acid or the polypeptide encoded by the claimed nucleic acid to be identical to the disclosed sequence and because the claims have no functional limitations.

For these reasons, which include the complexity and unpredictability of the nature of the invention and art in terms of the diversity of secreted and lack of knowledge about function(s) of encompassed nucleic acids structurally related to the nucleic acids encoding the polypeptide of SEQ ID NO: 2, the one limited working example of PRO241 polypeptide and its one function, the lack of direction or guidance for using the nucleic acids that are not identical to the disclosed nucleic acid sequence of SEQ ID NO: 1 or encoding the amino acid sequence of SEQ ID NO: 2, and the breadth of the claims for structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

7. Claims 22-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid having at least 80%, 85%, 90%, 95% or 99% sequence identity or hybridizing to a nucleic acid sequence encoding the polypeptide set forth in SEQ ID NO:2 or its fragments, to the nucleic acid sequence of SEQ ID NO: 1, or to the full-length coding sequence of the cDNA deposited under ATCC Accession No. 209526. The claims do not require that the nucleic acid or polypeptide encoded by the nucleic acid possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of nucleic acids that is defined only by sequence identity or hybridization.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying

characteristics, the specification does not provide adequate written description of the claimed genus.

In addition, claims 35-37 recite an isolated nucleic acid that hybridises to a nucleic acid sequence encoding the polypeptide set forth in SEQ ID NO: 2 or its fragments, to the nucleic acid sequence of SEQ ID NO: 1, or to the full-length coding sequence of the cDNA deposited under ATCC Accession No. 209526. Thus, the claims encompass a huge number of nucleic acids that vary substantially both in length and in nucleotide composition. In fact, the claims encompass virtually any random nucleic acid sequence of any length because the claims have no recitation of specific hybridization conditions and any nucleic acids could hybridize to the recited nucleic acids.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, an artisan cannot envision the detailed chemical structure of the encompassed genus of nucleic acids, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at

1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated nucleic acid encoding the polypeptide of SEQ ID NO: 2 (including the nucleic acid of SEQ ID NO: 1), but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115). It is suggested that a functional limitation be added to overcome the rejection.

Claim Rejections—35 USC § 112, 2nd paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 22-27, 30, 31, and 35-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-27, 30, 31, and 35-41 are indefinite because they recite the term "extracellular domains". The protein, identified as PRO241, with the amino acid sequence set forth in SEQ ID NO: 2 is a soluble protein, and is not disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed protein

comprises an "extracellular domain" is indefinite, as the art does not recognize soluble proteins as having such a domain.

Further, even if the protein had an extracellular domain, the recitation of "the extracellular domain, lacking its associated signal sequence" would still be found to be indefinite because a signal sequence is not generally considered to be part of an extracellular domain, as a signal sequence is cleaved from said domain in the process of secretion from a cell.

Claim 36 is indefinite also because they recite "under stringent conditions", without defining the hybridization conditions in the claims. Since neither the art nor the specification provides an unambiguous definition for the terms, the claims are indefinite.

Claim Rejections—35 USC § 102(b)

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 35-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Dreher et al. (GENEMBL, Accession No. U17834, January 5, 1995).

Dreher et al. teach a nucleotide sequence comprising 24 consecutive nucleotides that encode 8 amino acids of SEQ ID NO: 2 (See attached sequence alignment). The nucleotide sequence complementary to the nucleotide sequence of Dreher et al. would, by its nature, hybridize to the nucleic acid sequence encoding

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the polypeptide of SEQ ID NO: 2. Thus, the reference of Dreher et al. meets the limitations of claims 35-37.

Claim Objection

12. Claims 28, 29, and 32-34 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

13. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

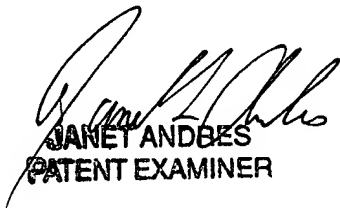
All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record

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includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on 2/25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ruixiang Li
Examiner
July 28, 2003



JANET ANDBES
PATENT EXAMINER